



CLAIMS

The invention in which an exclusive right is asserted is claimed as follows:

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1. A method for minimizing the aggregation tendencies of an amyloid forming protein,
the method comprising:
 - a) identifying a first amino acid sequence of the protein that is replaced by a
second amino acid sequence during physiological conditions; and
 - b) preventing the replacement by juxtaposing a peptide to the first amino acid
sequence.
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2. The method as recited in claim 1 wherein the method is conducted *in vivo*.
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2. The method as recited in claim 1 wherein the protein is a human protein selected from
the group consisting of human kappa-IV light chain variable domain and serine protease inhibitors.
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2. The method as recited in claim 3 wherein the peptide has an amino acid sequence
identical to an amino acid sequence in a region of the light chain variable domain.
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2. The method as recited in claim 3 wherein the peptide is inserted between residue
position numbers 60 and 83 of the protein.

1 6. The method as recited in claim 3 wherein the peptide has the amino acid sequence
2 Phe₇₁-Thr₇₂-Leu₇₃-Thr₇₄-Ile₇₅-Ser₇₆-Ser₇₇
3 and wherein the subscripts denote the positions of the amino acids in the domain.

1 7. The method as recited in claim 1 wherein the peptide is inserted when the protein is
2 partially unfolded.

1 8. The method as recited in claim 1 wherein the peptide is identical in composition to a
2 portion of the protein that anchors a hairpin-shaped amino acid sequence to the protein.

1 9. The method as recited in claim 1 wherein the protein is a greek key fold protein
2 selected from the group consisting of antibody constant domains, transthyretin, beta-2-microglobulin,
3 serine protease inhibitors, and crystalline.

1 10. The method as recited in claim 9 wherein the peptide is inserted at a hairpin anchorage
2 point in the greek key fold protein.

1 11. The method as recited in claim 1 wherein the peptide is a target for an endoplasmic
2 reticulum chaperone.

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A2 1 12. The method as recited in claim 1 wherein the peptide is an endoplasmic reticulum
2 chaperone selected from the group consisting of hsp70, hsc73 and BiP.

1 13. The method as recited in claim 1 wherein the peptide is a synthetic peptide selected
2 from the group consisting of TDFTLTI, FTLTISS, FTLKISR, FTLEISR, and LTLKLSR.

1 14. A peptide for insertion in an intact human kappa-IV light chain variable domain, the
2 peptide comprising the following amino acid sequence:

3 Phe₇₁-Thr₇₂-Leu₇₃-Thr₇₄-Ile₇₅-Ser₇₆-Ser₇₇

4 wherein the subscript numbers are the residue location points in the domain.

1 15. A method for preventing amyloid formation in human kappa-IV light chain variable
2 domain, the method comprising inserting the peptide Phe₇₁-Thr₇₂-Leu₇₃-Thr₇₄-Ile₇₅-Ser₇₆-Ser₇₇ into the
3 domain, wherein the subscript numbers indicate the residue location on the domain.

1 16. The method as recited in claim 15 wherein the domain is partially unfolded at the time
2 of insertion.

1 17. A method for preventing fibril assembly, the method comprising:
2 a) identifying a region of a first aggregating protein moiety that normally interacts
3 with a second protein moiety to form the assembly; and
4 b) juxtaposing a binding protein to the first moiety.

1 18. The method as recited in claim 17 wherein the first and second aggregating proteins
2 are immunoglobulin light chains.

1 19. The method as recited in claim 17 wherein the binding protein hybridizes with the
2 region.

1 20. The method as recited in claim 17 wherein the binding protein is an amino acid
2 sequence that is complementary to the amino acid sequence of the region.